

REMARKS

The foregoing amendment to the specification is supported in Figure 2A as originally filed and does not introduce new matter.

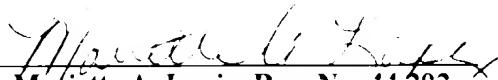
The amendment to Figure 2A merely adds a sequence identifier to the figure to comply with 37 C.F.R. 1.821(d) and does not introduce new matter.

Enclosed is a marked-up version of the changes made by this amendment. The enclosed pages are captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**"

Entry of the foregoing amendment is respectfully requested and favorable action on the merits is earnestly solicited.

Date: December 4, 2002

Respectfully submitted,

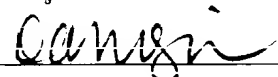
  
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**CERTIFICATE OF MAILING UNDER 37 CFR 1.8**

I hereby certify that this correspondence and its listed enclosures is being deposited with the United States Postal Service as First Class Mail, postage paid, in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231 on **December 4, 2002**

Name: **Deborah A. Mojarro**

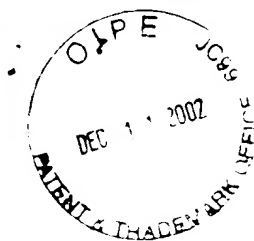
Signed: 

Date: 12/4/02

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

Page 8, lines 12-15 have been amended as follows:

Figure 2A-2B shows design of the targeting construct used to disrupt nuclear hormone receptor genes. Figure 2A, which illustrates the target sequence (SEQ ID NO:1) for the targeting construct, shows the location and extent of the disrupted portion of the nuclear hormone receptor gene, as well as the nucleotide sequences flanking the Neo' insert in the targeting construct. Figure 2B shows the sequences identified as SEQ ID NO:3 and SEQ ID NO:4, which were used as the targeting arms (homologous sequences) in the nuclear hormone receptor targeting construct.



# Construct

GI Number(s): 2267577

Gene Family: Nuclear Hormone Receptor

Gene

Subfamily: Orphan NHR

Gene Sequence: full-length cDNA, Mouse

underlined = deleted in targeting construct

[ ] = sequence flanking Neo insert in targeting construct

```
CCCTCGACCTCGAGATCCATTGTGCTCTAAAGCAGAGTCTGGGTCTACCTACATATGGC
ACCGAGGATACCTAGAGGCCCATGCAAGAGAAGGCCCTTGTCTTCCAGGCACTGAGGAC
CFCAGTCCCTAATTCTCTGGCACTTCTCTGAGATCTCAAGGAAAGCAGGGTCAAGCGAGGAGG
CCTGGGAGAGGAGGCATCCTACACCCAACTCTTGTGGCTCTCTCCCTAAGGSAACAGGA
GACCATGACAGCTATGCTAACACTAGAAACCATGGCCAGTGAAGAAGAATATGGGCCCGAG
GAAGTGTGTGGGTGTGGGAGACCTGGGCCACAGGCTATCATTTCCACGCGCTGACTTGTGA
GGGTGTGAAGGGCTCTCTCAGAGCAACATCAGCAAAACCATTTGGTCCCATCTGTCCGCTT
TCTCTGAAGGTGTGAGGTCAGCAAGGCCAGAGACGCCACTGTCCAGCCTGAGGTTGCA
GAAGTGTCTAAATGTGGGCATGAGGAAAGACATGATACTGTGAGCAGAAGCTCTGGCATT
GCGGTCAGCCAGACAGGCACAGCGCGGGCAGAGAAAGCATCTTTGCAACTGAATCAGCA
GCAGAAAGAACTGGTCCAGATCTCTCTGGGGGCCACACTCGCCATGTGGGCCCATTTGTT
TGACCAAGTTTGTGCAAGTTCAGGCTTCCAGCCTATCTGTTTCATGCATCACCGGCCCTTTCCA
GCTCTGGGGGCCCGTGTGCTCTGCTCACACACTTTGCAGATATCAACACGTTTATGGT
GCAACAGATCATCAAGTTCACCAAGGATCTGCGGCTCTTCCGGTCCCTAACCATGGAGGA
CCAGATCTCCCTTCTCAAGGGAGCGGCTGTGGAAATATGTCATATCTCACTCAACACTAC
CTTCTGTCTTCAAACAGAGAATTTCTCTGTGTGGGCTCTTTGCTACAAGATGGAGGACGG
AGTCCATGCAAGGTTCCAGTACGAGTTTGTGGAGTCGATCTCCACTTCCATAAAAAACCT
GAAAGGACTGCATCTCCAGGAGCCTGAGTATGTGCTCATGGCTGCCACGGGCCCTCTTCTC
CCCTGGTTTCTGTATGCAAAGCTGATGGGCTGCTGGCTGACCTCCGGAGTATAAACAAT
GCATACTCCTATGAAGTTCAGCGCTTGGAGGAACTGTCTGCTATGACGCCGCTGCTCGGG
GAGATTTGCAGTTGAGGCCAGGCTTGCATCCTTTCCCCAGACCCCCAGGGATACACTGG
CCTGGAAAGGTTACAGCGCTGGACCCCCACACAGCAGAAGGAGCTTGGGAGTGGCAATGAA
ATGCTGAACAGT
```

Gene Sequence  
Structure \*

282 bp

Sequence Deleted

403 bp

Size of full-length  
cDNA: 1332 bp



FIG. 2A



# Construct

GI Number(s): 2267577

Gene Family: Nuclear Hormone Receptor

Gene Subfamily: Orphan NHR

Gene Sequence: full-length cDNA, Mouse

underlined = deleted in targeting construct

[ ] = sequence flanking Neo insert in targeting construct

CCCTCGACCTCGAGATCCATTGTGCTCTAAAGCAGAGTCTGGGTCCTACCTACATATGGC  
ACCGAGGATACCTAGAGGCCCATGCAAGAGAAGGCCCTTGTTTTCCAGGCACTGAGGAC  
CGCAGTCCCTAATTCCTGGCAGTTCCCTGAGATCTCAAGGAAAGCAGGGTCAGCGAGGAGG  
CCTGGGGAGAGGAGGCATCCTACACCCAATCTTGTGGCCTGCTGCCTAAGGGAAACAGGA  
GACCATCAGCCTATCTTACACTAGAACCATGGCCAGTCAAGAGAAATATGGGGGAG  
GAAGTGTGTGGTGTGGTGGAGAGCGGGGCCACAGGCTATCATTTCCACGGCCCTGACTTGTGA  
GGGCTGGAAGGGGTTTCTTCAGAGCAACAGTCAGCAAAACCATTTGCTGCCATCTGTCCGTT  
TGCTGGAAGGTGTGAGGTCAAGCAAGGCCCCAGAGACGUCACGTCCAGCCTGCAGGTTGCA  
GAAGTGTCTAAATGTGGCATGAGGAAAGACATGATACTGTCAGCAGAAGCCCTGGCATT  
GCGGCGAGCCAGACAGGCACAGCGCGGGCAGAGAAAGCATCTTTGCAACTGAATCAGCA  
GCAGAAAGAACTGGTCCAGATCCTCCTGGGGGCCACACTCGCCATGTGGGGCCATTGTT  
TGACCAAGTTTGTGCACTTCAAGCCTCCAGCCTATCTGTTTCATGCATCACCGGCCTTTCCA  
GCCTCGGGGCCCCGTGTTGCCTCTGCTCACACACTTTGCAGATATCAACACGTTTATGGT  
GCAACAGATCATCAAGTTCACCAAGGATCTGCCGCTCTTCCGGTCCCTAACCATGGAGGA  
CCAGATCTCCCTTCTCAAGGGAGCGGCTGTGGAAATATTGCATATCTCACTCAACACTAC  
GTTCTGTCTTCAAACAGAGAATTTCTTCTGTGGGCCTCTTTGCTACAAGATGGAGGACGC  
AGTCCATGCAGGGTTCCAGTACGAGTTTGTGGAGTCGATCCTCCACTTCCATAAAAACCT  
GAAAGGACTGCATCTCCAGGAGCCTGAGTATGTGCTCATGGCTGCCACGGCCCTCTTCTC  
CCCTGGTTTTCTGTATGCAAAGCTGATGGGCCTGCTGGCTGACCTCCGGAGTATAAAACAAT  
GCATACTCCTATGAAGTTCAAGGCTTGGAGGAAGTGTCTGCTATGACGCCGCTGCTCGGG  
GAGATTTGCAGTTGAGGCCAGGCTTGATCCTTTCCCCAGACCCCCAGGGATACACTGG  
CCTGGAAAGGGTACAGCGCTGGACCCACACAGCAGAAGGAGCTTGGGAGTGGCAATGAA  
ATGCTGAACAGT (SEQ ID NO:1)

Gene Sequence  
Structure \*

282 bp

Sequence Deleted

403 bp

Size of full-length  
cDNA: 1332 bp



FIG. 2A